(FILE 'HOME' ENTERED AT 14:46:11 ON 02 JUN 95)

FILE 'HCA' ENTERED AT 14:46:43 ON 02 JUN 95
E EKINS/AU
L1 150 S E8-E11
L2 41182 S (MICROSPHERE? OR MICROCHIP? OR SUPERCHIP? OR BIOCHIP? O
L3 23 S L1 AND L2
E THERIAULT/AU
L4 4 S E57-E58
E CHU FRED/AU
L5 42 S E3-E7
L6 0 S L1 AND L4 AND L5
L7 0 S L1 AND L4
L8 7 S L1 AND L5
L9 0 S L4 AND L5

=> d cbib abs l8 1-7

L8 ANSWER 1 OF 7 HCA COPYRIGHT 1995 ACS
121:103239 Developing multianalyte assays. **Ekins, Roger P.**; **Chu, Frederick** (Med. Sch., Univ. Coll., London, W1N 8AA, UK). Trends Biotechnol., 12(3), 89-94 (English) 1994. CODEN: TRBIDM. ISSN: 0167-7799.
AB A review with 8 refs. Multianalyte 'binding' assays represent a major advance in microanal. technol. for the measurement of substances of biol. importance. Their further development should facilitate sensitive and reproducible quantification of analytes in many areas that are currently problematic, including diagnostic medicine and the standardization of biologicals.

L8 ANSWER 2 OF 7 HCA COPYRIGHT 1995 ACS
120:241888 Multianalyte microspot immunoassay. **Ekins, Roger**; **Chu, Frederick** (Med. Sch., Univ. Coll. London, London, W1N 8AA, UK). Anal. Proc., 30(12), 488-9 (English) 1993. CODEN: ANPRDI. ISSN: 0144-557X.
AB A review without refs. of the use of the multianalyte microspot immunoassay in immunodiagnosis.

L8 ANSWER 3 OF 7 HCA COPYRIGHT 1995 ACS
119:44689 Immunoassay or binding assay employing a capture binding agent and a developing binding agent conjugated to fluorescent dye-containing microspheres. **Ekins, Roger Philip**; **Chu, Frederick Woodnam** (Multilyte Ltd., UK). PCT Int. Appl. WO 9308472 A1 930429, 47 pp. DESIGNATED STATES: W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, UA, US; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 92-GB1892 921015. PRIORITY: GB 91-21873 911015; GB 92-21094 921007.
AB A high-sensitivity binding assay for an analyte, in which process a capture binding agent having binding sites specific for the analyte and a developing binding material capable of binding with the bound analyte or with the binding sites on the capture binding agent occupied by the bound analyte or with the binding sites remaining unoccupied on the capture binding agent are used, employs the capture binding agent in an amt. such that only an insignificant fraction of the analyte in the sample becomes bound to the capture binding agent, the capture binding agent preferably being present at high surface d. on microspots. A label is used in the assay in relation to the developing binding material, the label being provided by microspheres having a size of less than 5 .mu.m and

carrying a marker, preferably fluorescent dye m[illegible]. contained within the microspheres. Thus, an ultrasensitive sandwich 2-step back-titrn. TSH microspot immunoassay involves: (1) spotting polystyrene microtiter wells with .ltoreq.1 .mu.L monoclonal anti-TSH capture antibody, aspirating the antibody droplets, blocking the wells with bovine serum albumin, washing, adding 200 .mu.L sample to each well, and shaking the plate at room temp. for a given time (30 min to several h) and (2) adding 200 .mu.L developing binding material antibody conjugated to fluorescent dye-contg. latex microspheres (diam. 0.1 .mu.m), to each well, shaking the plate at room temp. for 0.5-1 h, washing, aspirating until completely dry, and scanning with an MRC-600 Laser Scanning Confocal Microscope. A binding assay for DNA using single-stranded oligonucleotide DNA probe (capture binding agent) and an antibody recognizing only twin-stranded DNA sequence or other developing binding material also is described.

L8 ANSWER 4 OF 7 HCA COPYRIGHT 1995 ACS
114:77971 Fluorescence spectroscopy and its application to a new generation of high sensitivity multi-microspot, multianalyte, immunoassay. **Ekins, Roger**; **Chu, Frederick**; Biggart, Elizabeth (Dep. Mol. Endocrinol., Univ. Coll., London, W1N 8AA, UK). Clin. Chim. Acta, 194(1), 91-114 (English) 1990. CODEN: CCATAR. ISSN: 0009-8981.
AB A review with 14 refs. Advantages of high sensitivity multi-microspot multianalyte immunoassay systems are discussed.

L8 ANSWER 5 OF 7 HCA COPYRIGHT 1995 ACS
112:94908 Development of microspot multianalyte ratiometric immunoassay using dual fluorescent-labelled antibodies. **Ekins, Roger**; **Chu, Frederick**; Biggart, Elizabeth (Dep. Mol. Endocrinol., Univ. Coll., London, W1N 8AA, UK). Anal. Chim. Acta, 227(1), 73-96 (English) 1989. CODEN: ACACAM. ISSN: 0003-2670.
AB The general principles underlying multianalyte microspot immunoassay methodol. are outlined. It relies on the measurement of the ratio of fluorescent signals from individual antibody microspots forming a microspot array on a suitable plastic surface. In principle, the methodol. is capable of measuring 106 different substances in a sample vol. of 100 .mu.L.

L8 ANSWER 6 OF 7 HCA COPYRIGHT 1995 ACS
112:3922 High specific activity chemiluminescent and fluorescent markers: their potential application to high sensitivity and 'multi-analyte' immunoassays. **Ekins, Roger**; **Chu, Frederick**; Micallef, Jacob (Univ. Coll., Univ. London, London, W1N 8AA, UK). J. Biolumin. Chemilumin., 4(1), 59-78 (English) 1989. CODEN: JBCHE7. ISSN: 0884-3996.
AB The sensitivities of immunoassays relying on conventional radioisotopic labels, i.e., RIA (RIA) and immunoradiometric assay (IRMA), permit the measurement of analyte concns. .gtorsim.107 mols./mL. This limitation primarily derives, in the case of competitive or limited reagent assays, from the manipulation errors arising in the system combined with the physicochem. characteristics of the particular antibody used; however, in the case of noncompetitive systems, the specific activity of the label may play a more important constraining role. It is theor. demonstrable that the development of assay techniques yielding detection limits significantly <107 mols./mL depends on the following: (1) the adoption of noncompetitive assays designs; (2) the use of labels of higher specific activity than radioisotopes; and (3) highly efficient discrimination between the products of the immunol. reactions involved. Chemiluminescent and fluorescent substances are

capable of yielding higher specific activities than commonly used radioisotopes when used as direct reagent labels in this context, and both thus provide a basis for the development of ultrasensitive, noncompetitive, immunoassay methodologies. Enzymes catalyzing chemiluminescent reactions or yielding fluorescent reaction products can likewise be used as labels yielding high effective specific activities and hence enhanced assay sensitivities. A particular advantage of fluorescent labels (albeit one not necessarily confined to them) lies in the possibility they offer of revealing immunol. reactions localized in microspots distributed on an inert solid support. This opens the way to the development of an entirely new generation of ambient analyte microspot immunoassays permitting the simultaneous measurement of tens or even hundreds of different analytes in the same small sample, using (for example) laser scanning techniques. Early experience suggests that microspot assays with sensitivities surpassing that of isotopically based methodologies can readily be developed.

L8 ANSWER 7 OF 7 HCA COPYRIGHT 1995 ACS

109:163730 Detection of corticosteroid binding globulin in parotid fluids: evidence for the presence of both protein-bound and non-protein-bound (free) steroids in uncontaminated saliva.

Chu, Frederick W.; **Ekins, R. P.** (Middx. Sch. Med., Univ. Coll., London, W1N 8AA, UK). Acta Endocrinol., 119(1), 56-60 (English) 1988. CODEN: ACENA7. ISSN: 0001-5598.

AB Corticosteroid-binding globulin (CBG) was detected by a specific RIA in mixed saliva (25.4 .mu.g/L) and in pure, uncontaminated parotid fluids (17.4 .mu.g/L) at resting flow-rates of approx. 500 .mu.L/min and 50 .mu.L/gland per min, resp. CBG was not detected in parotid fluids collected at stimulated flow-rates of 300-1000 .mu.L/gland per min. This suggested a flow-rate-dependent transfer/secretion of CBG in saliva. When cortisol was measured (RIA) in diln. expts. in both mixed saliva and parotid fluids using phosphate buffer at pH 7.4 as diluent, a protein-binding effect analogous to that found in plasma samples was obsd. However, this effect was abolished if a known CBG inhibitor, phosphate-citrate buffer at pH 4, was used as the diluent in the assay. A bound fraction of cortisol was found in both mixed saliva (14.0%) and parotid fluid samples (12.3%) by equil. dialysis. This contradicts the currently accepted notion that specific plasma steroid binding proteins (and protein-bound steroids) are absent from uncontaminated saliva, and that their presence in mixed saliva is the consequence solely of contamination by gingival fluid and/or plasma from mouth or gum abrasions. Apparently, both protein-bound and free steroids are present in uncontaminated saliva, so salivary total and plasma free steroid concns. are not identical.

=> fil home
FILE 'HOME' ENTERED AT 14:53:19 ON 02 JUN 95

```
     FILE 'MEDLINE' ENTERED AT 14:53:39 ON 02 JUN 95
                 E EKINS R/AU
L10           154 S E3,E5
                 E THERIAULT T/AU
L11             1 S E4
                 E CHU F/AU
L12            46 S E3
L13            10 S E18
L14             0 S L10 AND L11 AND (L12 OR L13)
L15             0 S L10 AND L11
L16             8 S L10 AND (L12 OR L13)
L17             0 S L11 AND (L12 OR L13)

=> d all l16 1-8

L16  ANSWER 1 OF 8  MEDLINE
AN   93161564     MEDLINE
TI   Multianalyte testing [letter].
AU   Ekins R; Chu F
SO   Clin Chem, (1993 Feb) 39 (2) 369-70.
     Journal code: DBZ. ISSN: 0009-9147.
CY   United States
DT   Letter
LA   English
FS   Priority Journals; Cancer Journals
EM   9305
CT   Check Tags: Human
     *Blood Chemical Analysis: MT, methods
      Blood Chemical Analysis: ST, standards
     *Immunoassay: MT, methods
      Immunoassay: ST, standards

L16  ANSWER 2 OF 8  MEDLINE
AN   93135371     MEDLINE
TI   Multianalyte microspot immunoassay. The microanalytical 'compact
     disk' of the future.
AU   Ekins R; Chu F
CS   Department of Molecular Endocrinology, University College and
     Middlesex School of Medicine, University College London, UK.
SO   Ann Biol Clin (Paris), (1992) 50 (5) 337-53.
     Journal code: 4ZS. ISSN: 0003-3898.
CY   France
DT   (DUPLICATE PUBLICATION)
     Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   9304
AB   Throughout the 1970s, controversy centered both on immunoassay
     'sensitivity' per se and on the relative sensitivities of labelled
     antibody and labelled analyte methods. Our own theoretical studies
     in this period revealed that radioimmunoassay (RIA) sensitivities
     could be surpassed only by the use of very high specific activity
     non-isotopic labels in 'non-competitive' designs, preferably based
     on the use of monoclonal antibodies. The time-resolved fluorescence
     methodology known as Delfia - developed in collaboration with the
     instrument manufacturer LKB/Wallac - represented the first
     commercial 'ultra-sensitive' non-isotopic technique based on these
     theoretical insights, the same concepts being subsequently adopted
     in comparable methodologies relying on the use of chemiluminescent
     and enzyme labels. However, a second advantage of high specific
     activity labels is that they permit the development of
```

'multi-analyte' immunoassay systems combining ultra-sensitivity with the simultaneous measurement of tens, hundreds or thousands of analytes in a small biological sample. This possibility relies on simple, albeit hitherto unexploited, physicochemical concepts. The first is that all immunoassays rely on measurement of Ab occupancy by analyte. The second is that, provided the Ab concentration used is 'vanishingly small', fractional Ab occupancy is independent of both Ab concentration and sample volume. This leads to the notion of 'ratiometric' immunoassay, involving measurement of the ratio of signals (eg fluorescent signals) emitted by two labelled Ab's, the first ('sensor' Ab) deposited as a microspot on a solid support, the second a 'developing' Ab directed against either occupied or unoccupied sensor Ab binding sites.(ABSTRACT TRUNCATED AT 250 WORDS)

CT Check Tags: Comparative Study; Human
Binding, Competitive
*Immunoassay
Immunoassay: MT, methods
Immunoassay: ST, standards

L16 ANSWER 3 OF 8 MEDLINE
AN 92035562 MEDLINE
TI Multianalyte microspot immunoassay--microanalytical "compact disk" of the future.
AU **Ekins R P; Chu F W**
CS Department of Molecular Endocrinology, University College and Middlesex School of Medicine, London, U.K.
SO Clin Chem, (1991 Nov) 37 (11) 1955-67. Ref: 29
Journal code: DBZ. ISSN: 0009-9147.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals; Cancer Journals
EM 9202
AB Throughout the 1970s, controversy centered both on immunoassay "sensitivity" per se and on the relative sensitivities of labeled antibody (Ab) and labeled analyte methods. Our theoretical studies revealed that RIA sensitivities could be surpassed only by the use of very high-specificity nonisotopic labels in "noncompetitive" designs, preferably with monoclonal antibodies. The time-resolved fluorescence methodology known as DELFIA--developed in collaboration with LKB/Wallac--represented the first commercial "ultrasensitive" nonisotopic technique based on these theoretical insights, the same concepts being subsequently adopted in comparable methodologies relying on the use of chemiluminescent and enzyme labels. However, high-specific-activity labels also permit the development of "multianalyte" immunoassay systems combining ultrasensitivity with the simultaneous measurement of tens, hundreds, or thousands of analytes in a small biological sample. This possibility relies on simple, albeit hitherto-unexploited, physicochemical concepts. The first is that all immunoassays rely on the measurement of Ab occupancy by analyte. The second is that, provided the Ab concentration used is "vanishingly small," fractional Ab occupancy is independent of both Ab concentration and sample volume. This leads to the notion of "ratiometric" immunoassay, involving measurement of the ratio of signals (e.g., fluorescent signals) emitted by two labeled Abs, the first (a "sensor" Ab) deposited as a microspot on a solid support, the second (a "developing" Ab) directed against either occupied or unoccupied binding sites of the sensor Ab. Our preliminary studies of this approach have relied on a dual-channel scanning-laser confocal microscope, permitting

microspots of area [redacted] microns 2 or less to be [redacted]lyzed, and implying that an array of 10(6) Ab-containing microspots, each directed against a different analyte, could, in principle, be accommodated on an area of 1 cm2. Although measurement of such analyte numbers is unlikely ever to be required, the ability to analyze biological fluids for a wide spectrum of analystes is likely to transform immunodiagnostics in the next decade.

CT Check Tags: Comparative Study; Human
Binding, Competitive
*Immunoassay
Immunoassay: MT, methods
Immunoassay: ST, standards

L16 ANSWER 4 OF 8 MEDLINE
AN 91282106 MEDLINE
TI Multispot, multianalyte, immunoassay.
AU **Ekins R**; **Chu F**; Biggart E
CS Department of Molecular Endocrinology, University College, Middlesex School of Medicine, London, UK.
SO Ann Biol Clin (Paris), (1990) 48 (9) 655-66.
Journal code: 4ZS. ISSN: 0003-3898.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9110
AB Consideration of the basic principles of immunoassay design reveals that highly sensitive assays can, in principle, be developed using amounts of "sensor" antibody far smaller than are currently conventional in this field. Furthermore, when using such amounts, the fractional occupancy of antibody binding sites by analyte is independent of both sample volume and antibody concentration. Labelling of both the sensor-antibody and a developing antibody (designed to recognize either occupied or unoccupied sensor-antibody binding sites) permits the development of "ratiometric" immunoassays relying on measurement of the ratio of signals emitted by the two labelled antibodies. Furthermore, the sensor-antibody can be located within a "microspot" a few microns 2 in area. By labelling both sensor and developing antibodies with fluorescent labels, and scanning the microspot using a highly focussed laser beam, microspot immunoassays at least comparable in sensitivity with conventional "macroscopic" immunoassays are made possible. This in turn permits the development of immunoassay "arrays" capable in principle of measuring very large numbers of different substances within small samples (such as a drop of blood). The general principles and theory underlying these concepts are discussed, and preliminary experimental data using currently available instrumentation reported.
CT Check Tags: Human; Support, Non-U.S. Gov't
Fluorescent Antibody Technique
*Immunoassay: MT, methods
Lasers: DU, diagnostic use
Sensitivity and Specificity

L16 ANSWER 5 OF 8 MEDLINE
AN 91160170 MEDLINE
TI Fluorescence spectroscopy and its application to a new generation of high sensitivity, multi-microspot, multianalyte, immunoassay.
AU **Ekins R**; **Chu F**; Biggart E
CS Department of Molecular Endocrinology, University College and Middlesex School of Medicine, London, UK.
SO Clin Chim Acta, (1990 Dec 17) 194 (1) 91-114.

Journal code: DCC SSN: 0009-8981.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9106
CT Check Tags: Human; Support, Non-U.S. Gov't
*Immunoassay: MT, methods
*Microscopy, Fluorescence

L16 ANSWER 6 OF 8 MEDLINE
AN 90022740 MEDLINE
TI High specific activity chemiluminescent and fluorescent markers: their potential application to high sensitivity and 'multi-analyte' immunoassays.
AU **Ekins R**; **Chu F**; Micallef J
CS Department of Molecular Endocrinology, University College, Middlesex School of Medicine, University of London, UK.
SO J Biolumin Chemilumin, (1989 Jul) 4 (1) 59-78.
Journal code: 129. ISSN: 0884-3996.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9001
AB The sensitivities of immunoassays relying on conventional radioisotopic labels (i.e. radioimmunoassay (RIA) and immunoradiometric assay (IRMA) permit the measurement of analyte concentrations above ca 10(7) molecules/ml. This limitation primarily derives, in the case of 'competitive' or 'limited reagent' assays, from the 'manipulation errors arising in the system combined with the physicochemical characteristics of the particular antibody used; however, in the case of 'non-competitive' systems, the specific activity of the label may play a more important constraining role. It is theoretically demonstrable that the development of assay techniques yielding detection limits significantly lower than 10(7) molecules/ml depends on: (1) the adoption of 'non-competitive' assays designs; (2) the use of labels of higher specific activity than radioisotopes; (3) highly efficient discrimination between the products of the immunological reactions involved. Chemiluminescent and fluorescent substances are capable of yielding higher specific activities than commonly used radioisotopes when used as direct reagent labels in this context, and both thus provide a basis for the development of 'ultra-sensitive', non-competitive, immunoassay methodologies. Enzymes catalysing chemiluminescent reactions or yielding fluorescent reaction products can likewise be used as labels yielding high effective specific activities and hence enhanced assay sensitivities. A particular advantage of fluorescent labels (albeit one not necessarily confined to them) lies in the possibility they offer of revealing immunological reactions localized in 'microspots' distributed on an inert solid support. This opens the way to the development of an entirely new generation of 'ambient analyte' microspot immunoassays permitting the simultaneous measurement of tens or even hundreds of different analytes in the same small sample, using (for example) laser scanning techniques. Early experience suggests that microspot assays with sensitivities surpassing that of isotopically based methodologies can readily be developed.
CT Check Tags: Support, Non-U.S. Gov't
Antibody Affinity
Binding, Competitive
*Fluorescent Dyes

*Immunoassay: MT, methods
*Luminescence
Radioimmunoassay: MT, methods
CN 0 (Fluorescent Dyes)

L16 ANSWER 7 OF 8 MEDLINE
AN 89267759 MEDLINE
TI Validity of current analog-based free hormone immunoassays.
AU Jowett T; **Chu F; Ekins R**
CS Department of Molecular Endocrinology, Middlesex Hospital Medical School, University of London.
SO Steroids, (1988 Oct) 52 (4) 365-6.
Journal code: V10. ISSN: 0039-128X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8909
CT Blood Proteins: ME, metabolism
*Hormones: AN, analysis
*Hormones, Synthetic: DU, diagnostic use
Immunoassay
Protein Binding
CN 0 (Blood Proteins); 0 (Hormones)

L16 ANSWER 8 OF 8 MEDLINE
AN 88323587 MEDLINE
TI Detection of corticosteroid binding globulin in parotid fluids: evidence for the presence of both protein-bound and non-protein-bound (free) steroids in uncontaminated saliva.
AU **Chu F W; Ekins R P**
CS Department of Molecular Endocrinology, University College, London, UK.
SO Acta Endocrinol (Copenh), (1988 Sep) 119 (1) 56-60.
Journal code: 0NC. ISSN: 0001-5598.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8812
AB Corticosteroid binding globulin (CBG) was detected by a specific radioimmunoassay in mixed saliva (25.4 +/- 4.0 micrograms/l, mean +/- SEM) and in pure, uncontaminated parotid fluids (17.4 +/- 2.7 micrograms/l) at resting flow-rates of approximately 500 microliters/min and 50 microliters/gland per min, respectively. In parotid fluids collected at stimulated flow-rates of between 300-1000 microliters/gland per min, CBG could not be detected. This observation suggests the direct flow-rate-dependent transfer/secretion of CBG in saliva. When cortisol was measured (RIA) in dilution experiments in both mixed saliva and parotid fluids using phosphate buffer at pH 7.4 as diluent, a protein-binding effect analogous to that found in plasma samples was observed. However, this effect was abolished if a known CBG inhibitor, phosphate:citrate buffer at pH 4, was used as the diluent in the assay. A bound fraction of cortisol was found in both mixed saliva (14.0 +/- 4.0%) and parotid fluid samples (12.3 +/- 1.3%) by equilibrium dialysis. These findings appear to contradict the currently accepted notion that specific plasma steroid binding proteins, and hence the protein-bound steroids, are absent in uncontaminated saliva; and that their presence in mixed saliva is the consequence solely of contamination by gingival fluid and/or plasma from mouth or gum abrasions. We conclude that both

protein-bound and free steroids are present in uncontaminated saliva and that salivary total and plasma free steroid concentrations are not identical.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Adult
*Exudates and Transudates: ME, metabolism
Hydrocortisone: ME, metabolism
*Parotid Gland: ME, metabolism
Protein Binding
Radioimmunoassay
*Saliva: ME, metabolism
*Transcortin: ME, metabolism

RN 50-23-7 (Hydrocortisone); 9010-38-2 (Transcortin)

=> file home
FILE 'HOME' ENTERED AT 15:00:24 ON 02 JUN 95

This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☒ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☐ FADED TEXT OR DRAWING
- ☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☐ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☒ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.
As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.